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Ambient Water Quality Criteria Document Addendum for 2,4-Dichlorophenol

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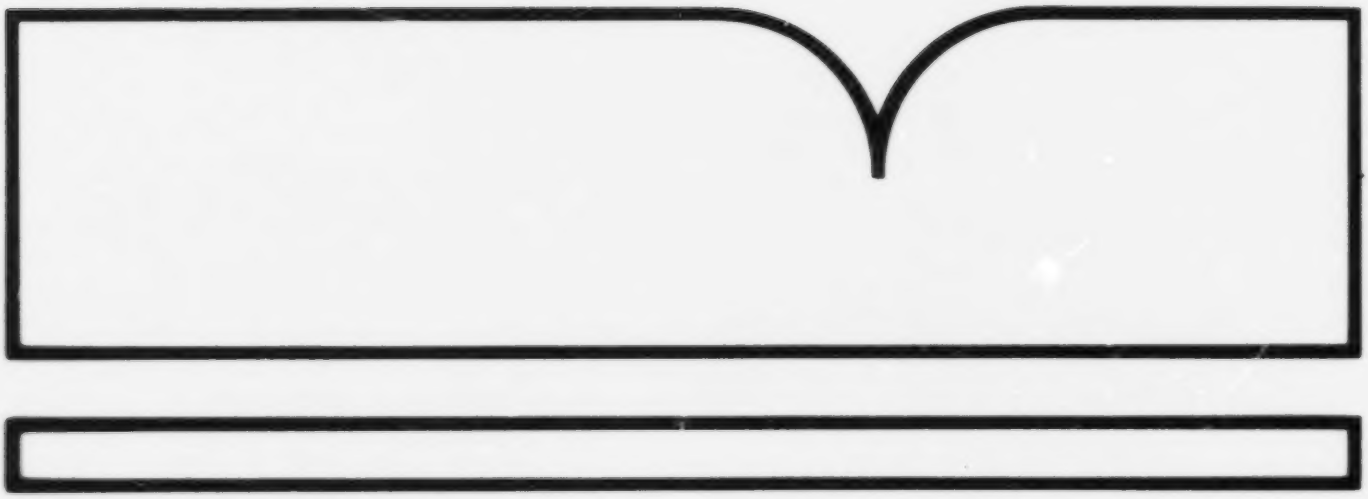

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ADDENDUM FOR 2,4-DICHLOROPHENOL

Prepared for

OFFICE OF WATER REGULATIONS
AND STANDARDS

Prepared by

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Under the 1977 Clean Water Act, Congress mandated the U.S. Environmental Protection Agency to develop ambient water quality criteria for 129 priority Pollutants. These criteria were published in 1980. Under Section 304(a)(1) of the Clean Water Act as amended in 1987, the U.S. EPA is mandated to re-evaluate and update these criteria every five jears. These addenda represent an updated literature search current as of 1988, plus additional information from Agency files and Program Offices. This addendum is to update the existing Ambient Water Quality Criteria Document for 2, 4-Dichlorophenol.

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PREFACE

Under the 1977 Clean Water Act, Congress mandated the U.S. Environmental Protection Agency to develop ambient water quality criteria for 129 priority pollutants. These criteria were published in 1980. Under Section 304(a)(1) of the Clean Water Act as amended in 1987, the U.S. EPA is mandated to re-evaluate and update these criteria every five years. These addenda represent an updated literature search current as of 1988, plus additional information from Agency files and Program Offices. The first draft of this addendum was prepared by Syracuse Research Corporation under contract no. 68-C8-0004.

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
CRAVE	Carcinogen Risk Assessment Verification Endeavor
LOAEL	Lowest-observed-adverse-effect level
NOAEL	No-observed-adverse-effect level
ppm	Parts per million
RfD	Reference dose
RQ	Reportable quantity
SGOT	Serum glutamic oxaloacetic transaminase
SGPT	Serum glutamic pyruvic transaminase

INTRODUCTION

Under Section 304(a)(1) of the Clean Water Act of 1977 as amended in 1987, the U.S. EPA is required to publish criteria for water quality accurately reflecting the latest scientific knowledge regarding the effects on health and welfare that may occur from the presence of pollutants in any body of water, including groundwater. In accordance with the 1977 act, Ambient Water Quality Criteria Documents (AWQCDs) were developed in 1980 for 65 toxic pollutants or classes of pollutants listed under Section 307(a)(1).

These addenda are intended to serve as an update of the original AWQCDs. The addenda provide the Agency with the latest scientific assessments of potential health hazards associated with these pollutants and serve as guidelines for modifying the current (1980) AWQCDs.

The human health criteria in these addenda are based on Agency verified risk assessment values when available. These values consist of reference doses (RfD) for those chemicals believed to be systemic toxicants (i.e., do not induce cancer) and cancer risk factors for those thought likely to cause cancer in humans. The verification process consists of a review and consensus of risk assessment values provided by an Agency workgroup consisting of scientists from each of the major Agency offices. Assessments for noncarcinogens are verified by the RfD workgroup and those for carcinogens are verified by the Carcinogen Risk Assessment Verification Endeavor (CRAVE) workgroup. If such values are not available, the criteria are based on the most recent Agency health assessment. In the absence of any appropriate Agency value, RfD values or cancer risk factors are derived by current Agency methods if adequate new data are available, and criteria are recommended based on the proposed RfD or risk factor.

The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfD is derived by dividing a NOAEL or LOAEL for subchronic or chronic exposure by standard uncertainty factor(s) times an additional uncertainty factor:

$$RfD = \frac{\text{NOAEL or LOAEL}}{UF(s) \times UF}$$

The standard uncertainty factors are applied to reflect the various types of data used to estimate RfDs. An uncertainty factor of 10 is used to account for variations in human sensitivity when extrapolating from valid human studies involving long-term exposure of average, healthy subjects. An additional 10-fold factor is used for each of the following: to extrapolate from long-term animal studies to the case of humans, to extrapolate from subchronic animal studies to chronic exposure, and to extrapolate from a LOAEL to a NOAEL. An additional uncertainty factor of >0-10 may be applied to reflect professional assessment of the uncertainties of the study and data base not explicitly addressed by the standard uncertainty factors (i.e., completeness of the overall data base). The default value for the additional uncertainty factor is 1.

In assessing the carcinogenic potential of a chemical, the U.S. EPA classifies the chemical into one of the following groups according to the degree of evidence in epidemiological studies and animal studies: Group A - Human Carcinogen; Group B - Probable Human Carcinogen [limited evidence in humans with or without sufficient evidence in animals (Group B1) or inadequate evidence in humans with sufficient evidence in animals (Group B2)]; Group C - Possible Human Carcinogen (limited evidence of carcinogenicity in animals in the absence of human data); Group D - Not Classifiable as to

Human Carcinogenicity (inadequate or no evidence); Group E - Evidence of Noncarcinogenicity for Humans. Quantitative carcinogenic risk assessments are performed for chemicals in Groups A and B, and on a case-by-case basis for chemicals in Group C. Upper-bound cancer unit risks (slope values) are estimated through the use of mathematical extrapolation models. Most commonly for animal data, the linearized multistage model with a 95% upper confidence limit is used to provide a low-dose estimate of cancer risk. The cancer risk is characterized as an upper-limit estimate (i.e., the true risk to humans, while not identifiable, is not likely to exceed the upper-limit estimate and in fact may be lower). Alternative risk models to the multistage model, such as the one-hit, Weibull, Logit or Probit model, are available and may be used when the evidence indicates that they may be more appropriate. In the absence of such evidence, the Agency recommends the linearized multistage model to provide consistency of approach and an upper-bound on the potential carcinogenic risk. In the case where human data are used for quantitative risk assessment, an upper-bound estimate rather than a 95% upper-bound estimate is used when low-dose linearity is assumed.

In the development of this Addendum to the AWQCD on 2,4-dichlorophenol, recent Agency assessments have been consulted. A computerized literature search was conducted to cover studies published more recently than the latest Agency assessment (i.e., published in 1985 to 1988). New key studies have been evaluated.

REVIEW OF NEW DATA

Toxicologic/Carcinogenic Effects

Minimal health effects data exist on the chronic toxicity or carcinogenicity of 2,4-DCP. Only one chronic study (Exon and Koller, 1985) has been published since the publication of the 1980 AWQCD on 2,4-DCP. In that study, negative results for carcinogenicity and cocarcinogenicity were reported for 2,4-dichlorophenol. Female Sprague-Dawley rats were exposed to 0, 3, 30 or 300 ppm 2,4-dichlorophenol (98% purity) in drinking water from 3 weeks of age through breeding, parturition and lactation. The authors estimated the exposure to be -0, 0.3, 3.0 and 30 mg/kg/day. The offspring (24-32/sex/exposure level) of these animals were continued on the same treatment until tumor development or until termination of the experiment at 24 months. Microscopic examination of major organs did not reveal increased tumor incidences, decreased latency to tumor formation or variation in tumor type in treated rats compared with controls.

Exon and Koller (1985) also reported the effects of pre- and postnatal exposure to 2,4-dichlorophenol on the immune response system. Female Sprague-Dawley rats were exposed to 2,4-dichlorophenol as described above. Progeny of these animals (10 pups/group) were exposed through weanling $\geq$15 weeks of age. Immunologic assays for humoral immunity, cell-mediated immunity and macrophage function were performed, along with body, liver, spleen and thymus weight measurements. No effects were seen at 3 ppm. There appeared to be a dose related increase in serum antibody level response to keyhole limpet hemocyanin which was significantly increased at the 300 ppm dose. Delayed hypersensitivity responses, elicited by sensitizing with bovine serum albumin emulsified in Freund's complete adjuvant

and injected subcutaneously at the base of the tail, were decreased significantly at 30 ppm 2,4-dichlorophenol. Macrophage test results were similar to those of the controls. Liver and spleen weights were significantly increased at 300 ppm. Thymus weights were consistently, though not significantly, reduced. There was no change in body weights.

Reproductive indices (percent conception, litter size, number of stillborn, birth and weaning weight and survival to weaning) were also examined by Exon and Koller (1985). Female weanling Sprague-Dawley rats (12-14/dose) were exposed to 0, 3, 30 or 300 ppm 2,4-dichlorophenol in the drinking water from 3 weeks of age through breeding (at 90 days to untreated males) and parturition. Litter sizes were reduced significantly at 300 ppm, and percent stillborn pups appeared to be dose related, but did not differ significantly from controls at the highest dose tested. Survival to weaning was reduced significantly at 30 ppm.

Seyler et al. (1984) exposed male CD-1 mice for 90 days to 0, 50, 150 or 500 mg/kg in drinking water and found no decrease in sperm motility or ability to penetrate ova. Also, in vitro exposure had no effect on these characteristics.

Kobayashi et al. (1972) fed 2,4-dichlorophenol in the diet to male ICR mice for 6 months. Behavior, growth rate, hematological values, SGOT and SGPT endpoints were evaluated. Slight unfavorable effects were reported in the liver at 230 mg/kg/day. No effects were noted at 100 mg/kg/day.

No human data on the adverse health effects of oral exposure to chlorophenols, specifically 2,4-DCP, could be found in the available literature. Occupational studies of workers by inhalation and dermal routes have resulted in headache, dizziness, weakness, nausea and paresthesias.

Chloracne and acquired porphyria were observed in workers engaged in the manufacturing of 2,4-DCP and 2,4,5-TCP. Exposure of the workers included acetic acid, phenol, and monochloroacetic acid as well as intermediates used in the manufacture of the finished products 2,4-DCP and 2,4,5-TCP; therefore, no conclusions could be drawn from these results.

Bioconcentration Factor (BCF)

Pertinent new information concerning the bioconcentration factor for 2,4-dichlorophenol is currently undergong Agency review. The BCF value of 40.7 determined in U.S. EPA (1980) will be used until this review is completed.

QUANTIFICATION OF EFFECTS

The ambient water quality criterion for 2.4-dichlorophenol recommended by U.S. EPA (1980) was 0.3 µg/ℓ, based upon organoleptic factors (odor and taste). The criteria based upon toxicological data would have been 3.09 mg/ℓ (U.S. EPA, 1980), and for fish consumption only, 26.46 mg/ℓ. These values were based upon an ADI of 7 mg/day, 0.0065 kg fish and shellfish consumed/day, a BCF of 40.7, 2 ℓ drinking water consumed/day, and an average human adult weight of 70 kg. The ADI was derived from a NOAEL of 100 mg/kg/day established in a chronic mouse oral study by Kobayashi et al. (1972). U.S. EPA (1988) lists the ambient water quality criteria derived from toxicity data as 3.09 mg/ℓ, both for water and fish consumption and for fish consumption only.

Recent data published by Exon and Koller (1985) have been used as the basis for the verified oral RfD, 0.003 mg/kg/day (U.S. EPA, 1986). A NOAEL of 3 ppm in drinking water (0.3 mg/kg/day) and a LOAEL of 30 ppm in drinking water (3.0 mg/kg/day) for immunotoxicity were identified in rats (Exon and Koller, 1985). No increase in tumor incidences was reported.

Based on these data and data reviewed in the U.S. EPA (1980), the U.S. EPA (1987a,b) classified 2,4-dichlorophenol in U.S. EPA group D - not classifiable as to human carcinogenicity.

Using the verified oral RfD of 0.003 mg/kg/day, assuming an average human water consumption of 2 ℓ/day and fish and shellfish consumption of 6.5 g/day, a 70 kg average adult weight, and using a BCF of 40.7 for 2,4-dichlorophenol, the criterion for consumption of water and fish and shellfish is 0.093 mg/ℓ. For consumption of fish and shellfish only the criterion is 0.79 mg/ℓ.

EXISTING STANDARDS AND CRITERIA

An oral RfD for 2,4-dichlorophenol of 0.003 mg/kg/day has been verified (U.S. EPA. 1986) and is based on a rat study by Exon and Koller (1985).

The U.S. EPA (1988) determined the final RQ for 2,4-dichlorophenol to be 100 pounds, based on aquatic toxicity.

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